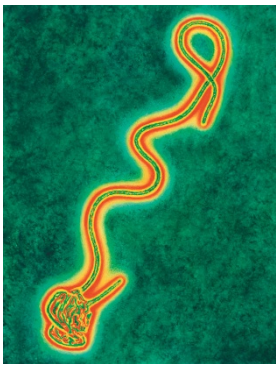
Spit pill for Ebola



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An anticoagulant drug derived from nematode saliva counteracts Ebola in rhesus macaques, according to preliminary findings by Thomas Geisbert *et al.* in the 13 December *Lancet*. The drug prevented death in three out of nine macaques and prolonged the life of the remaining six. The virus is normally nearly 100% fatal in macaques, and about 80% fatal in humans.

The investigators homed in on this drug after earlier studies indicated that Ebola virus triggers overexpression of tissue factor, a procoagulant protein. This overexpression contributes to the coagulation abnormalities that accompany Ebola infection and can lead to organ failure and death.

The drug, recombinant nematode anticoagulant protein (rNAPc2), interferes with the tissue factor complex, and is derived from parasitic hookworms that use the protein to keep their hosts liquid. The rNAPc2 protein seems to be safe, according to results of phase 2 clinical trials designed to prevent clot formation in patients undergoing knee replacement or angioplasty. The drug may be the most promising candidate for the intractable Ebola, and might also be helpful against other hemorrhagic fevers.

I am *B. thetaiotaomicron*; I come in peace

Our digestive tracts coexist peacefully with commensal microbes which help provide nutrients and maintain health. A study in the January *Nature Immunology* reveals the basis for this coexistence with one prevalent bacterium, *Bacteroides thetaiotaomicron.*

Infection by pathogens normally prompts a swift immunological kick, initiated by host 'pattern-recognition' receptors such as toll-like receptors. Symbiotic bacteria have many of the same molecular patterns that induce the inflammatory response to pathogenic bacteria, yet somehow the host accepts the symbionts.

Denise Kelly *et al.* found that acceptance of these bacteria depends on molecular events that occur after activation of pattern-recognition receptors—namely, activation of NF-κB. Translocation of NF-κB to the nucleus induces transcription of numerous proinflammatory genes, including cytokines, chemokines and adhesion molecules. The investigators found that exposure of gut epithelial cells to *B. thetaiotaomicron* flushed NF-κB out of the nucleus. This seems to occur through a *Bacteroides*-induced nuclear association between a subunit of NF-κB and the nuclear hormone receptor PPAR-γ. Association of the two proteins promotes nuclear export.

Previous studies have found that avirulent *Salmonella* strains can also inhibit NF-κB activity, but through an entirely different mechanism. These strains prevent translocation of NF-κB into the nucleus by interfering with degradation of IκB, which sequesters NF-κB in the cytoplasm.

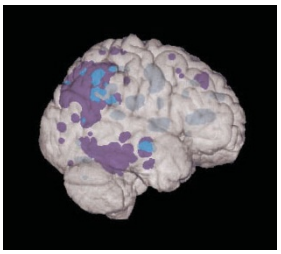
Several studies indicate that patients with inflammatory bowel disease initiate abnormal inflammatory responses to commensal bacteria. Whether cells in these patients also fail to properly regulate NF-κB remains to be seen.

Written by Charlotte Schubert

Power in repetition

Small microsatellite DNA repeats get out of hand in a number of neurological diseases. In the rare inherited neuromuscular disorder myotonic dystrophy (DM), CTG or CCTG repeats can be duplicated up to 11,000 times in the non-coding region of a single locus. A study in the 12 December *Science* examines the consequences of this profligacy. One theory holds that, in DM, repeat expansions sequester RNA-binding proteins. This theory has been borne out in mouse models that express a large CTG repeat in the 3′ UTR of the human skeletal actin transgene. These transgenes, which accumulate in the nucleus, bind proteins in the muscleblind gene family. Researchers have speculated that sequestration of muscleblind proteins affects splicing of other genes, such as those that maintain muscle integrity. Until now, no one had asked whether mice lacking muscleblind also have symptoms of DM. Rahul Kanadia *et al.* found that they do. Moreover, mice lacking one of several muscleblind genes showed aberrant splicing of genes affected in DM. The new findings bolster the notion that DM results from sequestration of specific RNA-binding proteins by an expansion of a repetitive element.

APOE's sugar low



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People with the apolipoprotein ε4 allele—about a quarter of the population—have an increased risk of Alzheimer disease (AD) later in life. Eric Reiman *et al.* now find that these individuals also show impaired glucose metabolism in the same regions of the brain as AD patients, decades before the possible onset of cognitive problems. In the December 15 online *PNAS* the investigators imaged glucose metabolism in 12 ε4 carriers and 15 noncarriers, aged 20–39. Regions of low glucose metabolism in carriers overlapped with regions affected in AD patients (purple, areas low only in AD patients; muted blue, areas affected only in carriers; bright blue, regions of overlap). The data bring researchers closer to the source of cognitive decline, although it is unclear whether such measurements could be used to predict Alzheimer disease. In fact, half of ε4 heterozygotes are unlikely to develop AD, and the average age of onset seems to be in the seventh decade of life.

IL-10 tames transplantation

Individuals on deck for a bone marrow transplant must go through a battery of tests to see how well they match up with potential donors. A report in the December 4 *NEJM* suggests that they might also soon be tested for polymorphisms in the gene encoding interleukin-10 (IL-10), which suppresses the production of inflammatory mediators and promotes immunological tolerance. Previous studies had suggested that one common IL-10 variant boosted IL-10 production and seemed to shield patients from graft-versus-host-disease (GVHD). Ming-Tseh Lin *et al.* examined 993 transplant patients and their HLA–identical siblings, and found that patients with this variant had a reduced risk of GVHD and death. In white individuals, the variant is present in about a quarter of the population, but in Japanese populations the frequency reaches about 70%. Curiously, Japanese transplant recipients also have a lower incidence of GVHD.